STIC-ILL

519874

From: Citation@cas.org
Sent: Friday, November 26, 2004 4:59 PM
To: STIC-ILL
Subject: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

ChemPort

Send a colleague this Reference

From

1644

MAHER HADDAD (via **ChemPort**)
571 272-0845
maher.haddad@uspto.gov

15679711

Comments

10/030,522

COMPLETED

Dialog 135

Document Citation

Title: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

Author(s):

Source: Blood Weekly, (9 Sep 1996) pp. N/A. ISSN: 1065-6073.

Full-Text Options

Access your document options via **ChemPort**!

DL NO

If you have any questions regarding **ChemPort**, or require assistance retrieving your Full-text Options, please contact the Help Desk.

STIC-ILL

From: Citation@cas.org

Sent: Friday, November 26, 2004 5:00 PM

To: STIC-ILL

Subject: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

ChemPort

Send a colleague this Reference

From

MAHER HADDAD (via **ChemPort**)
571 272-0845
maher.haddad@uspto.gov

Comments

10/030,522

Document Citation

Title: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

Author(s):

Source: Blood Weekly, (9 Sep 1996) . ISSN: 1065-6073.

Full-Text Options

Access your document options via **ChemPort**!

If you have any questions regarding **ChemPort**, or require assistance retrieving your Full-text Options, please contact the Help Desk.

5/9/1 (Item 1 from file: 135)

0000009651 (THIS IS THE FULLTEXT)

"Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

Blood Weekly, September 9, 1996, p.17

DOCUMENT TYPE: Research News LANGUAGE: English
RECORD TYPE: FULLTEXT
AUDIENCE: Professional
Word Count:
373

TEXT: According to an abstract submitted by the authors to the 22nd International Congress of the World Federation of Hemophilia, held June 23-28, 1996, in Dublin, Ireland, "Eight to 20% of haemophilia A patients produce antibodies neutralizing the activity of infused factor VIII. Determination of the specificity of those antibodies is a critical requisite for the understanding of the mechanisms sustaining immune response towards FVIII and the design of new therapies to inhibit the activity of anti-FVIII antibodies or suppress their production. So far, the analysis of the specificity of anti-FVIII antibodies has been carried out with human polyclonal antibodies which is rendered difficult by the large repertoire of those antibodies. Such study would be greatly facilitated by the use of human monoclonal anti-FVIII antibodies provided the monoclonal antibodies reflect exactly the repertoire of the patient's antibodies. For this purpose we have established cell lines producing human IgG anti-FVIII monoclonal antibodies by immortalizing with the Epstein Barr virus B lymphocytes from a hemophilia A patient with inhibitor. Lymphocytes were purified from the blood of the hemophilia A patient with known inhibitor and immortalized by infection with Epstein-Barr virus. Supernatants were screened in ELISA for the presence of IgG anti-FVIII antibodies. Cell lines in positive wells were expanded and cloned. The selection of cell lines producing antibodies of the IgG isotype ensures that the antibodies accurately reflect the specificity of the patient's immune response. Indeed IgG antibodies are produced by memory B lymphocytes by opposition to IgM antibodies that are produced mostly by naive B cells. The supernatants of immortalized cell lines producing IgG anti-FVIII antibodies were then tested for their ability to inhibit FVIII activity. Two cell lines producing neutralizing anti-FVIII antibodies were expanded and subcloned. Both cell lines recognized the light chain of FVIII on Western blot as did the polyclonal antibodies present in the patients plasma. These results indicate that the production of human monoclonal antibodies by the Epstein-Barr virus technique is a promising approach to study FVIII inhibitor." (Authors) B. Desqueper, M. Jacquemin, J. Arnout, M. DiGiambatista, J.G. Gilles, R. Laub, K. Peerlinck, J. Vermylen and J.-M. Saint-Remy. (Institution) Center for Molecular and Vascular Biology, Leuven, Belgium.

DESCRIPTORS: news
SUBJECT HEADING: Pathogenesis (Haemophilia)

```
=> d his

     (FILE 'HOME' ENTERED AT 16:10:18 ON 26 NOV 2004)

     FILE 'DISSABS, 1MOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
     COMPUAB, CONF, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, LIFESCI, MEDICONF,
     OCEAN, PAPERCHEM2, PASCAL, POLLUAB, SOLIDSTATE, ADISCTI, ADISINSIGHT,
     ADISNEWS, ANABSTR, ANTE, AQUALINE, BIOBUSINESS, ...' ENTERED AT 16:10:30
     ON 26 NOV 2004
L1            32 S LE2E9
L2            11 DUP REM L1 (21 DUPLICATES REMOVED)
L3            22 S KRIX (A) 1
L4            14 DUP REM L3 (8 DUPLICATES REMOVED)
L5            69 S  BO2C11
L6            26 DUP REM L5 (43 DUPLICATES REMOVED)
L7         47166 S HUMAN (A) ((MONOCLONAL ANTIBOD?) OR MAB)
L8            47 S (L7 (S) FVIII)
L9            19 DUP REM L8 (28 DUPLICATES REMOVED)
```

ACCESSION NUMBER: 96:474329 PROMT
TITLE: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."
SOURCE: Blood Weekly, (9 Sep 1996) pp. N/A.
ISSN: 1065-6073.
LANGUAGE: English
WORD COUNT: 359
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB B. Desqueper, M. Jacquemin, J. Arnout, M. DiGiambatista, J.G. Gilles, R. Laub, K. Peerlinck, J. Vermylen and J.-M. Saint-Remy. Center for Molecular and Vascular Biology, Leuven, Belgium.
According to an abstract submitted by the authors to the 22nd International Congress of the World Federation of Hemophilia, held June 23-28, 1996, in Dublin, Ireland, "Eight to 20% of haemophilia A patients produce antibodies neutralizing the activity of infused factor VIII. Determination of the specificity of those antibodies is a critical requisite for the understanding of the mechanisms sustaining immune response towards **FVIII** and the design of new therapies to inhibit the activity of anti-**FVIII** antibodies or suppress their production. So far, the analysis of the specificity of anti-**FVIII** antibodies has been carried out with human polyclonal antibodies which is rendered difficult by the large repertoire of those antibodies. Such study would be greatly facilitated by the use of human monoclonal anti-**FVIII** antibodies provided the monoclonal antibodies reflect exactly the repertoire of the patient's antibodies. For this purpose we have established cell lines producing human IgG anti-**FVIII** monoclonal antibodies by immortalizing with the Epstein Barr virus B lymphocytes from a hemophilia A patient with inhibitor. Lymphocytes were purified from the blood of the hemophilia A patient with known inhibitor and immortalized by infection with Epstein-Barr virus. Supernatants were screened in ELISA for the presence of IgG anti-**FVIII** antibodies. Cell lines in positive wells were expanded and cloned. The selection of cell lines producing antibodies of the IgG isotype ensures that the antibodies accurately reflect the specificity of the patient's immune response. Indeed IgG antibodies are produced by memory B lymphocytes by opposition to IgM antibodies that are produced mostly by naive B cells. The supernatants of immortalized cell lines producing IgG anti-**FVIII** antibodies were then tested for their ability to inhibit **FVIII** activity. Two cell lines producing neutralizing anti-**FVIII** antibodies were expanded and subcloned. Both cell lines recognized the light chain of **FVIII** on Western blot as did the polyclonal antibodies present in the patients plasma. These results indicate that the production of **human monoclonal antibodies** by the Epstein-Barr virus technique is a promising approach to study **FVIII** inhibitor."

Cell lines in positive wells were expanded and cloned. The selection of cell lines producing antibodies of the IgG. . . opposition to IgM antibodies that are produced mostly by naive B cells. The supernatants of immortalized cell lines producing IgG anti-**FVIII** antibodies were then tested for their ability to inhibit **FVIII** activity. Two cell lines producing neutralizing anti-**FVIII** antibodies were expanded and subcloned. Both cell lines recognized the light chain of **FVIII** on Western blot as did the polyclonal antibodies present in the patients plasma. These results indicate that the production of **human monoclonal antibodies** by the Epstein-Barr virus technique is a promising approach to study **FVIII** inhibitor."